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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/074,250	02/14/2002	Laura E. Niklason	1579-637	5073

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EXAMINER	
CHONG, YONG SOO	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 04/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/074,250	NIKLASON ET AL.	
	Examiner	Art Unit	
	Yong S. Chong	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23 and 28* is/are pending in the application.

4a) Of the above claim(s) *2-9,12-23 and 28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 10-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

This Office Action is in response to applicant's arguments filed on 2/2/2006. Claims 2-9, 12-23, 28 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected species, of record in the Office Action dated 12/15/2003. Claims 1-23, 28 are pending. Claims 1, 10-11 are examined herein. Applicant's arguments have been fully considered but found not persuasive for reasons of record. The rejections are repeated below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 1 12, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventions, at the time the application was filed, had full possession of the claimed invention.

The claims herein are drawn to the use of any therapeutic agents represented by "an agent that inhibits vascular cell proliferation" and "a chemotherapeutic agent". These recitations, are seen to be merely functional language.

Thus, the recitations in the claim are deemed to a broad genus of any compounds represented by "an agent that inhibits vascular cell proliferation" and "a

chemotherapeutic agent" which would reasonably be interpreted to encompass those known and unknown compounds having the recited functions as of the instant filing date. Note those future known compounds yet to be discovered and/or made. Hence, those unknown or future known compounds encompassed by claim 1 herein must required to additional or future research to discover, establish or verify their usefulness..

The specification as originally filed does not provide adequate support for the generic claims herein. The specification merely describes particular inhibits vascular cell proliferation or particular chemotherapeutic agent disclosed in claim 11 . The specification has not taught any other agents are intended to be encompassed within the scope of claims.

Functional language at the point of novelty, as herein employed by Applicants, is admoiished in University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (CAFC, 1997) at 1406: stating this usage does "little more than outline goal appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate". The CAFC further clearly states that "(A) written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, or chemical name, of the claimed subject matter sufficient to distinguish it from other materials" at 1405 (emphasis added), and that "It does not define any structural features commonly possessed by members of the genus that distinguish from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identitv of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the

genus.." at 1406 (emphases added).

The court of *In re Curtis* also held that "a patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when... the evidence indicates ordinary artisans could not predict the operability .....of any other species." (see *In re Curtis* 354 F.3d 1347, 69 USPQ2d 1274, Fed. Cir. 2004). The court of Noelle v. Lederman also pointed out that generic claim to anti-CD40CR Mabs lacked written description support because there was no description of anti-human or other species Mabs, an no description of human CD40CR antigen. The court further pointed out that attempt to "define an unknown by its binding affinity to another unknown" failed. See 355 F.3d 1343, 69 USPQ2d 1508, Fed. Cir. 2004.

In this case, the claimed functional language is deemed not to adequately described by particular compounds in claim 11 . Thus, ordinary artisans could not predict the operability of any known and unknown compounds encompassed by the claim. Thus, the claimed method is seen to clearly lack of written description.

Claim 1 is rejected under 35 U.S.C. 1 12, first paragraph, for lack of scope of enablement because the specification, while being enabling for the particular agent or compound that inhibits vascular cell proliferation or particular chemotherapeutic agent disclosed in claim 11 for example and the specification for the claimed method herein, does not reasonably provide enablement for any compounds for inhibiting vascular cell proliferatipn, for the same reasons of record in the Office Action July 28, 2004.

These recitations, "an agent that inhibits vascular cell proliferation" and "a chemotherapeutic agenr', are seen to be merely functional language.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without undue experimentation. Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman* 230 USPQ 546 (BdApls 1 986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art', (5) the breadth of the claims; (6) the amount of direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary.

The nature of the invention: The instant invention pertains to a method of treating cerebral vasopasm that accompanies subarachnoid hemorrhage in a patient.

The relative skill of those in the art: The relative skill of those in the art is high.

The breadth of the claims: The instant claims are deemed very broad since the broadest claim (i.e., claim 10) reads on any compounds represented by "an agent that inhibits vascular cell proliferation" and "a chemotherapeutic agent" employed in the method herein.

The amount of direction or guidance presented:

Functional language at the point of novelty, as herein employed by Applicants, is admonished in University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (CAFC,

1997) at 1406: stating this usage does "little more than outline goal appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate." The CAFC further clearly states that "(A) written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, or chemical name, of the claimed subject matter sumcient to distinguish it from other materials" at l4 (emphasis added), and that "It does not define any structural features commonly possessed by members of the genus that distinguish from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identitv of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus.." at 1406 (emphases added).

In the instant case, "an agent that inhibits vascular cell proliferation" and “a chemotherapeutic agent", recited in the instant claims are purely functional distinction. Hence, these functional recitations read on any compounds that might have the recited functions. However, the specification merely provides one particular compound for each kind of functional compounds in the specification.

Thus, Applicants functional language at the point of novelty fails to meet the requirements set forth under 35 U.S.C. 1 12, first paragraph. Claims employing functional language at the exact point of novelty, such as Applicants', neither provide those elements required to practice the inventions, nor "inform the public during the life of the patent of the limited of monopoly asserted" (General Electric Company v. Wabash Appliance Corporation et al. 37 USPQ at 468 (US Supreme Court 1938)).

The predictabilitv or unpredictability: the instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art cannot fully described genus, visualize or recognize the identity of the members of the genus, by structure, formula, or chemical name, of the claimed subject matter, as discussed above in University of California v. Eli Lilly and Co. Hence, in the absence of fully recognizing the identity of the members genus herein, one of skill in the art would be unable to fully predict possible physiological activities of any compounds having claimed functional properties in the pharmaceutical compositions herein.

Moreover, one of skill in the art would recognize that it is highly unpredictable in regard to therapeutic effects, side effects, and especially serious toxicity that may be generated by drug-drug interactions when and/or after administering to a host (e.g., a human) any compounds represented by "an agent that inhibits vascular cell proliferation" and "a chemotherapeutic agent" which may encompass more than a thousand compounds. See text book. "Goodman & Gilman's The Pharmacological Basis of Therapeutics" regarding possible drug-drug interactions (9th ed, 1996) page 51 in particular. This book teaches that "The frequency of significant beneficial or adverse drug interactions is unknown" (see the bottom of the left column of page 51) and that

"Recognition of beneficial effects and 'recognition of and prevention of adverse drug interactions require a thorough knowledge of the intended and possible effects of drugs that are prescribed" and that 'The most important adverse drug-drug interactions occur with drugs that have serious toxicity and a low therapeutic index, such that relatively small changes in drug level can have significant adverse consequences" (see the right column of page 51) (emphases added). In the instant case, in the absence of fully recognizing the identity of the members genus herein, one of skill in the art would not be able to fully predict possible adverse drug-drug interactions occurring with many combinations of any compounds having claimed functional properties in the pharmaceutical compositions herein to be administered to a host. Thus, the teachings of the book clearly support that the instant claimed invention is highly unpredictable.

The presence or absence of working examples and the quantity of experimentation necessary:

As discussed above, only those particular agents are disclosed in the specification. Moreover, it is noted that the specification fails to provide working examples, i.e., testing results or data to demonstrate that any chemotherapeutic agent or methotrexate to be administered to a host, i.e., in vitro or vivo, in treating for cerebral vasopasm in a patient.

Thus, the specification fails to provide sufficient support of the broad use of any compounds represented by "an agent that inhibits vascular cell proliferation" and "a chemotherapeutic agent" recited in the instant claims. As a result, necessitating one of skill to perform an exhaustive search for the embodiments of any compounds having

those functions recited in the instant claims suitable to practice the claimed invention.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors, the case University of California v. Eli Lilly and Co. (CAFC, 1997) and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test all compounds encompassed in the instant claims employed in the claimed method to be administered to a host, with no assurance of success.

Response to Argument

Applicant's arguments filed 2/2/06 with respect to this rejection made under 35 U.S.C. 112, first paragraph, for lack of full scope of enablement have been fully considered but are not deemed persuasive as further discussed below.

Applicants argue that the novelty of the claimed methods results not from the specific nature of the agent used, but rather from the fact that Applicants were the first to appreciate and discloses that narrowing of cerebral arteries that is characteristic of cerebral vasospasm is in fact due to proliferation of cells in the vascular wall and/or accumulation of extracellular matrix under the influence of growth factors". Applicants' arguments are not found convincing.

First, the primary and critical method step in the claimed method is directed to

administer "an agent that inhibits vascular cell proliferation" or "a chemotherapeutic agent" to a patient in need of such treatment (see claim 1, the independent claim, and claims 10-11). Thus, what and which agent to be administered to the patient in this method step for the particular treatment is deemed to be crucial and critical. Hence this method step is indeed at the exact point of novelty.

Second, what Applicants argue and assert herein, i.e., "narrowing of cerebral arteries that is characteristic of cerebral vasospasm is in fact due to proliferation of cells in the vascular wall and/or accumulation of extracellular matrix under the influence of growth factors" is deemed merely the mechanism of action of a treatment. Note that the mechanism of action of a treatment does not have a bearing on the patentability of the invention if the method steps are already known even though applicant has proposed or claimed the mechanism.

Moreover, Applicants' assertions that at pages 7-10 of the application, a large number and wide variety of suitable agents are described" and that "no exhausted search for compounds would be required, have been considered but not found convincing. As noted in MPEP 2111, during patent examination, claims are given their broadest reasonable interpretation. It is proper to use the specification to interpret what the applicant meant by a word or phrase recited in the claim, However, it is not proper to read limitations appearing in the specification into the claim when these limitations are not recited in the claim. See In re Paulsen, 30 F.3d 1475, 1480, 31 USPQ2d 1671, 1674 (Fed. Cir. 1994) for example.

In this case, as discussed in the previous Office Action, the instant claim 1 read

on administering to a patient any compound represented by "an agent that inhibits vascular cell proliferation" and "a chemotherapeutic agent". These recitations broadly encompass those known and unknown compounds having the recited functions as of the instant filing date. Note those future known compounds yet to be discovered and/or made. Hence, those unknown or future known compounds encompassed by claim 1 herein must required to additional or future research to discover, establish or verify their usefulness. Therefore, as indicated in the previous Office Action, the skilled artisan has to exercise undue experimentation to practice the instant invention.

Applicants further argue that the relevance of the Examiner's comment on page 6 of the Action relating to drug-drug interaction is not seen. The purpose of discussing the possible therapeutic effects, side effects, and especially serious toxicitv that may be generated by drug-drug interactions when administering any compounds represented by "an agent that inhibits vascular cell proliferation" or "a chemotherapeutic agent" to a patient having vascular cell proliferation (a cancer patient), is to illustrate the unpredictability of the claimed method in claim 1 herein, since one of skill in the art would acknowledge that a cancer patient often receives multiple chemotherapeutic treatments by administering more than one chemotherapeutic agent. In the absence of fully recognizing the identity of the members genus herein, the agent herein, one of skill in the art would not be able to fully predict possible adverse drug-drug interactions occurring with the agent herein in combination with other chemotherapeutic agents to be administered to a cancer patient. Thus, the teachings of the book clearly support that the instant claimed invention is highly unpredictable.

Therefore, in view of the Wands factors discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test all compounds encompassed in the instant claims and their use in the claimed method, with no assurance of success.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 10-11 are rejected under 38 U.S.C. 102(b) as being anticipated by Black (US Patent 5,527,778).

Black discloses that well-known neuropharmaceutical agents such as chemotherapeutic agents, in particular, methotrexate (see col.4 line 57 to col.5 line 10) to be administered to a patient are useful in methods of treating abnormal brain tissue including subarachnoid hemorrhage, head injury (head trauma) and cerebral ischemia, and opening abnormal brain tissue capillaries in a patient, i.e., a mammal (see abstract, col.4 lines 1-9).

Thus, the disclosure of Black anticipates claims 1 and 10-11.

Response to Argument

Applicant's arguments filed 2/2/06 with respect to this rejection made under 35 U.S.C. 102(b) have been fully considered but are not deemed persuasive as fudher discussed below.

Applicants argue that the syndrome is characterized by diffuse narrowing of cerebral arteries in the general region of the SAH and that the present invention relates to method of treating, or inhibiting progression of, this complication/syndrome... resulting in risk of subsequent stroke. Thus, Applicants conclude that the citation would in no' way have suggested the presently claimed approach to testing, or inhibiting progression of, the cerebral vasospasm complication of SAH that Applicants have realized is due to the proliferation of cells in the vascular wall and/or accumulation of extracellular matrix. Applicant's arguments are not found persuasive for the following reasons.

What Applicants asserd herein is deemed to be merely the proposed or claimed mechanism of action of the treatment. Note that the mechanism of action of a treatment does not have a bearing on the patentability of the invention if the method steps are already known, i.e., administering methotrexate to the same patient herein having brain tumors or cancers (see abstract of Black's patent) even though applicant has proposed or claimed the mechanism. Applicant's recitation of a new mechanism of action for the prior art method will not, by itself, distinguish the instant claims over the prior art teaching the same or nearly the same method steps. Further, the claiming of a new use, new function or unknown property which is inherently present in the prior art method will not make the claim patentable as set forth in the 102(b) rejection above. Moreover,

mere recognition of latent properties in the prior art does not render novel or nonobvious an otherwise known invention. See *In re Wiseman*, 201 USPQ 658 (CCPA 1979).

For the above stated reasons, said claims are properly rejected under 35 U.S.C. 102(b). Therefore, said rejection is adhered to.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

YSC

SHENGJUN WANG
PRIMARY EXAMINER